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Everett L. Hodges

July 5, 1990



Mr. James Caldwell
Chief Fuels Section
U.S. Environmental Protection Agency
Field Exploration & Support Division
EN397
Fairchild Building
Washington, D.C. 20460

Dear James:

I was asked at the Hearing last week if there was information relative to blood/manganese in individuals exposed to environmental manganese. The answer is "yes". Enclosed is a study performed by Dr. John Cawte, et al regarding the Groote Eylandt manganese intoxication exposure of the Aboriginees versus Whites in the area.

Would you please see that the proper parties receive a copy.

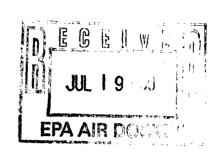
Very truly yours,

Everett L. "Red" Hodges

ELH: 1m

Encl.





"DO NATIVES OF AUSTRALIA VARY AS STRANGELY AS ITS SOIL"?— EXPLORATIONS ON THE FRONTIERS OF LAND-DWELLERS' RESPONSES TO MINERAL EXSPOSURES.

John Cawte

John Cawte A.O., M.D., Ph.D., F.R.A.N.Z.C.P. Professor of Psychiatry, Health Services Development, Prince of Wales Hospital, Randwick N.S.W. 2034

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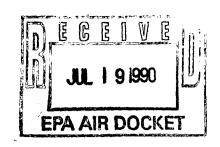
ABSTRACT

"The natives of Australia vary as strangely as its soil"

Commander J. Lort Stokes, R.N., H.M.S. Beagle, 1843.

This venerable truism is nowhere more evident than in the vicinity of Blue Mud Bay, a vast expanse of East Arnhem Land in north Australia, explored in the early nineteenth centuries by ships of the Royal Navy, H.M.S. <u>Investigator</u> and H.M.S. <u>Beagle</u>. Three clusters of neuro-psychiatric disorders affect certain of the traditional dwellers of this region, which includes Groote Evidence is presented that these afflictions may be related to the land in which they are accustomed to live, which assails them with mineral extremes. The first cluster is a congenital affliction, with lax joint ligaments associated with some lower motor neurone signs. The second cluster is an adult disorder of pyramidal, spinocerebellar and extrapyramidal tracts, These two disorders are mostly which may be progressive. The third cluster is a temperamental irritability, familial. with quick violence, which calls for an inordinate need for police intervention to manage it.

No ready diagnostic formula is available for these disorders. Undoubtedly multifactorial, they may represent responses by clans that possess a familial susceptibility to local ecotoxins, which include high levels of manganese and aluminium, often with low levels of iron and calcium. Features of the Blue Mud Bay disorders are reviewed, and compared and contrasted with modern concepts of manganese ecotoxicity as it may be described, or inferred, elsewhere in the world. Australian papers expressing our findings in this subject have mostly been published in technical journals (1).



BLUE MUD BAY: HISTORICAL NOTES OF HUMAN ECOLOGY AND ECOTOXICITY

Blue Mud Bay, with the adjacent East Arnhem Land coast and its islands, covers about half of the western coastal area of the Gulf of Carpentaria, in North Australia. Its bearings are 137 south latitude. The prevailing blue mud was noted by Lt. Matthew Flinders, R.N., during his epic circumnavigation of Terra Australis. Flinders entered it into his log on the day of Saturday, 22nd January, 1803, and charted it (Map 1) quite accurately for those times. He wrote:

"The bottom here, and in most other parts of the bay, is a blue mud of so fine a quality, that I judge it might be useful in the manufacture of earthern ware; and I thence named this Blue-mud Bay".

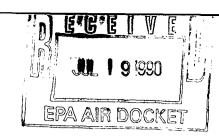
Flinders was partly right; manganese came to be used as a dye for glass and soaps, but he could not have foreseen the importance that this element would possess for modern industry, or its significance for modern medicine, where its metabolic role is only now being elucidated.

Flinders night logically have named Arnhem Bay, "Red Mud Bay". It reveals the aluminium ore (bauxite) that is also a feature of East Arnhem Land, constituting another potential hazard for Land-Dwellers. But by this time, the whole crew of H.M.S. Investigator was suffering from scurvy, and Matthew Flinders was forced to curtail his voyage and sail to Timor.

How do the native inhabitants of Blue Mud Bay and East Arnhem Land, exposed throughout their lifetimes to an ecology permeated by manganese, manage to survive the ill effects which such an exposure might predict? Divalent manganese, the predominant form, is substantially non-toxic. Trivalent manganese is very toxic due to the oxidation that occurs in its presence in the basal ganglia and throughout the motor neurones generally. Factors that facilitate the attack of trivalent manganese upon the catecholamines (1) are well known.

This paper will summarise some of the writer's observations of people of East Arnhem Land, dwelling in blue mud and red mud, made over the past ten years, at their invitation. It offers no solution to difficult medical problems, but hopefully brings us nearer to that goal.

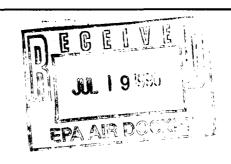
Before embarking on modern observations, however, some of the initial signs noted by Matthew Flinders aboard H.M.S. Investigator in 1803 are worth recalling for our purpose. Flinders' journals are fortunately available to the general reader through Australiana Facsimile Editions, reproduced by Librarian Board of South Australia from a copy held in the Public Library of South Australia.



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MAP 1. Chart by Matthew Flinders of the Blue Mud Bay region, made in 1803





The events of Flinders' passage during his days in Blue Mud Bay are beset with some of the highest dramas of his voyages: dramas which surely indicate something about the temperament of the local inhabitants. He notes, inter alia:

"It does not accord with the usually timid character of the natives of Terra Australis, to suppose the Indians came over from Isle Woodah for the purpose of making an attack; yet the circumstances of their being without women or children - their following so briskly after Mr. Woodall - and advancing armed to the wooders, all imply that they rather sought than avoided a quarrel. I can account for this unusual conduct only by supposing, that they might have has differences with, and entertained no respectful opinion of the Asiatic visitors, of whom we had found so many traces, some almost in sight of this place".

This brief extract from <u>Investigator's</u> log hardly does justice to the unusual "Indian" reactivity and excitability apparent in the disposition of these inhabitants, whom the voyagers unsuccessfully sought to placate. Flinders' narrative provides data for the student of temperament of the people.

The scientific research ship H.M.S. <u>Beagle</u> (famed as the observation platform of Charles Darwin, on a prior voyage) is usually given the credit of establishing that the colour of Blue Mud Bay is due to its high content of manganese. However, the journal of <u>Beagle's</u> Captain, Commander J. Lort Stokes, R.N., (1) makes no mention of this analysis in the pages of another facsimile edition from the Librarian Board of South Australia, entitled:

Discoveries in Australia, with an account of the coasts and rivers explored and surveyed during the voyage of H.M.S. Beagle in the years 1837-43. Despite a detailed account of the southern coast of the Gulf of Carpentaria, there seems, in this facsimile edition, an omission of Stokes' observations of the west coast, including the portentous Blue Mud Bay. In another part of his manuscript, dealing with the Illawarra region, Stokes' comment is worth citing for present purposes: "The natives of Australia vary as strangely as its soil". Stokes' was referring particularly to temperament.

The geological distribution of manganese is not precisely known. Core drilling have shown high deposits in East Arnhem Land as far west as Lake Evella and north as Caledon Bay (Map 2). A doctor has two other ways of checking local exposure. Traditional artists liked to use the valued ore (pyrolusite) on bark paintings (Fig. 1). It makes a blacker background than the charcoal used elsewhere. Groote Eylandt artists used it generally and mainland artists occasionally. Whether the ore was imported or local might be hard to tell. A more specific method is to estimate blood or hair levels of manganese. This has



proved positive on the mainland extending west and north of Blue Mud Bay. Exposure to manganese, while perhaps most marked at Groote Eylandt, is not limited to that site. Manganese is incorporated into a widespread ecology and food chain. So is aluminium. Low levels of calcium in the nutrition might lead to a secondary hyperparathyroidism with deposition of these metals, as well as calcium, in the intra and extra-neuronal spaces.

SUSCEPTIBILITY TO MANGANESE TOXICITY: A KEY TOPIC

This paper will focus predominantly on the most ominous metallic excess, manganese. An apparent idiosyncrasy of human reactivity to manganese is that the majority of those who are exposed to the metal sustain no harm. Workers, with a lifetime of contact, remain in good health but certain individuals become affected neurologically after a few months. The conclusion is that the latter individuals are genetically sensitive, or have encountered co-factors that alter the normal handling of manganese by oxidation and excretion.

Dr. Patrick Macleod (1) at the Centre for Medical Genetics at Queen's University of Kingston, Ontario, Canada, researches a rare disease called Joseph Machado syndrome, which affects with parkinsonism and related signs families of Azorean (Portuguese) ancestry in California and New York. He contends that there is a genetic susceptibility to ecotoxic agents, based on the interplay between a specific gene and the environment in terms of oxidation. He distinguishes clinically between extensive metabolizers (E.M's) and poor metabolizers (P.M.'s). Among the Chile manganese miners, he suggests that slow or poor metabolizers comprise the minority affected by manganese dust.

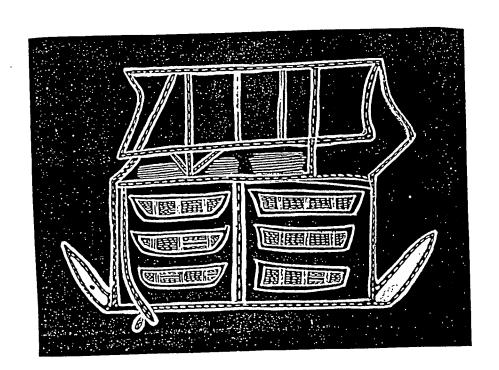
According to Macleod, one way of distinguishing the slow metabolizers in a community is based on testing with caffeine (through a bottle of Coca-Cola) followed by urine sampling. A better way, he now suggests, is to use a cough syrup containing dextro-methorphan, produced by Parke Davis, and sold over the counter. This provides a safe and non-intrusive test for poor or slow oxidisers.

This method of finding poor metabolisers (P.M.'s) will be tested by a manganese ecotoxicologist, also from Ontario, Canada, Dr. John Donaldson if who will work in conjunction with local researcher Dr. Tim Burt at Groote Eylandt later in 1990.

Only a proportion of the indigenous inhabitants of the Blue Mud Bay region seems susceptible to neurological patterns that could conceivably be related to the surrounding manganese. The individual susceptibility seems to be mainly limited to three extended families, locally called clans, which may be designated here as clans 3, L and Y. Cases occurring outside these clans are exceptional. This indicates a strong genetic susceptibility.



FIGURE 1

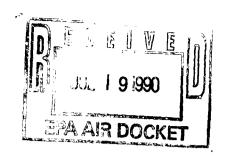


The Malay Prau of Bakunda

From Time Before Morning by Louis Allen, 1975.

Crowell Co., New York.

The usual black background, made from ore, features a great Macassan ship, anchored to the beach, laden with dug-out canoes.



The signs and symptoms shown by affected individuals in clans B, L and Y will be indicated, after an introductory review of symptomatology of manganese in the outside world. This is a field that may be expanding of late, moving outside the area of industrial medicine, so that it is becoming a subject of wider medical and psychiatric concern since the contemporary information was presented to a Darwin conference in 1987 (3).

RECENT EXTENSIONS OF MANGANESE SYMPTOMATOLOGY

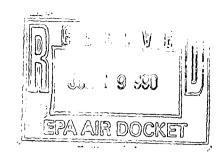
Manganese susceptibility has long been recognised by medicine. It was at the time of H.M.S. Beagle's voyages that manganese was first recognised as being neurotoxic. Couper (6) noted in 1837 that neurological effects sometimes ensued in workers in a mill where black oxide of manganese was inhaled into the lungs. Since then, toxicity has been progressively reported in miners in Chile, Morocco, Cuba, India, U.S.S.R. and U.S.A. Australian miners, in open-cut mines conducted by The Groote Eylandt Mining Company, a subsidiary of B.H.P., seem to have escaped. company now observes safety precautions against the inevitable exposure to dust, such as air-conditioned cabins for the working vehicles. However, pyrolusite screenings have been used to fill holes in community roads in Angurugu, and in one case, in a children's playpen in Alyangula, the company town, indicating that earlier caution was less than rigorous.

The majority of cases of manganism reported in the literature come from industry rather than from mining. The metal is used in the manufacture of ferro-manganese alloys, dry battery cells, paints, varnishes and enamels, and in the process of colouring glass and soaps.

In Canada today, all these traditional uses are now exceeded by the use of a manganese compound as an antiknock agent in the production of lead-free gasoline ⁽⁵⁾. It is widely presumed that the greatest commercial use of manganese in Australia may likewise be in lead-free petrol, but the petroleum corporations have made no public announcement.

classical medical literature, Reviewing clinical signs manganese toxicity are described as emerging in a small percentage of individuals exposed to manganese dust for a period of six months or longer. In miners, though apparently not in manufacturers, there may occur an acute and transient excited response, with emotional instability, and easy arousal to aberrant behaviour including violence. This syndrome, which seems not to have been carefully observed or described, has been called "locura manganica" or manganese madness. A classical recollection is of one sufferer running after a tram and beating it with his fists (!).

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Chronic intoxication, however, is well described in the literature ((*)((*)(*))). The complaint of asthenia is predominantly followed by extrapyramidal signs. Rigidity, drooling and insomnia occur. Impotence has been noted. The syndrome, indicating basal ganglia damage, is not a consistent one. It appears to be described with variation in different locations, such as Morocco or Japan ((*)(*)(*)).

Administration of L Dopa was found in cases studied by George Cotzias (11)(16) to effect improvement. However, the improvement was apparently not sustained, despite the clearance of tissue manganese concentrations.

A new prospective risk confronting those susceptible to manganese recently emerged through findings in prisons in U.S.A. of significantly elevated manganese levels in the hair of violent prisoners, compared with non-violent prisoners (17). observers of this phenomenon are concerned that violent prisoners, those having high manganese markers in the hair, may be let out of jail after completing their sentences, while nobody treats them or follows them up (11). While this observation is not as yet established forensic science, it seems to have been enough to cause a deferral by oil corporations in the U.S.A. from adding manganese compounds to gasoline as an anti-knock, a procedure which would increase pollution by the metal around roads and highways. Combustible gasoline boosters, such as ethanol and methanol, are available for gasoline, though they may be more costly for petroleum corporations.

Any presumed linkage between raised environmental manganese at Groote Eylandt (Tables 1 and 2), genetic susceptibility to this metal, and temperamental behaviour, requires more research in the light of these findings.

NEUROLOGICAL SYNDROMES IN EAST ARNHEM LAND

No autopsy material is available in East Arnhem Land to support a possible linkage between neurological illness and high manganese exposure, associated perhaps with endogenous co-factors such as high levels of aluminium (bauxite) and low levels of calcium and iron. Therefore, the symptoms in the clans affected, B, L and Y, need careful analysis to evaluate their similarity to or difference from, syndromes described elsewhere.

Many of the affected individuals show higher levels of blood manganese than average (Table 3). This is not a diagnostic indicator. A high level generally indicates recent exposure, rather than a poor metabolizer (PM) status.



TABLE 1. MANGANESE IN AIR AND WATER

(Courtesy T.M. Florence, D.Sc., of CSIRO)

SAMPLE	<u>ANGURUGU</u>	SYDNEY	WORLD AVERAGE
Tapwater, ugMn/L	4.3(8/85) 70(1/87)	5.8	-
Angurugu River, ugMn/L	27(8/85) 97(1/87)	-	8(for rivers)
Air, ugMn/m¹	23(3m from road) 1.2(10m from road)	0.05	0.04 (European)

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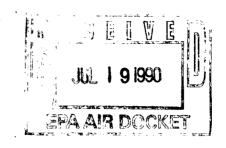
TABLE 2. MANGANESE IN TRADITIONAL FOOD SOURCES COLLECTION FROM OLD CARDEN AREAS*

(Courtesy T.M. Florence, D.Sc., of CSIRO)

SAMPLE	ugMn/g fresh weight		
	ANGURUGU	SYDNEY	
Fish, Angurugu River	36	0.3	
Oysters, Mud Cod Bay	0.25	0.05	
Yam, young	657	5**	
Yam, old	484	5**	
Citrus fruit	0.85	0.3	
Banana	79	1.5	
Billy Tea	6.7	-	

^{*} U.S. intake: range 2-9 mgMn/day, mean, 3.7 mg/day.

^{**} Root vegetables.



TABLES 3

Manganese found in whole blood in 26 individuals at three townships of Groote Eylandt (Note: initials have been coded to protect identity).

	Initials	Age	CNS Disease	Blood Mn. n mol/l
Aborigines in Angurugu	I.M. L.M. T.M. S.N. S.B.N. Q.S. H.X. T.N. U.M.	Adult Adult Adult Adult Adult Infant Adult Adult Adult Adult Adult	Yes Yes No Yes Yes Yes No No No	630 640 390 710 660 465 180 305 320 770
Caucasians in Angurugu	M.L. D.L. K.X. M.E.	Adult Adult Adult Adult	No No No No	105 90 160 175
Aborigines in Umbakumba	E.C. N.C.	Adult Adult	Yes Yes	285 170
Caucasians in Alyangula	U.U. B.X. C.K. K.O. H.B. E.O. M.C. N.U. L.X. E.T.	Adult Adult Adult Adult Adult Adult Adult Adult Adult	No	405# 110 180 165 230 195 125 115 140

Note:

Trace metal chemists have advised us of two references ranges for this metal: 100-350 n mol/L, and 100-500 n

mol/L.
This surprisingly high level, in an apparently well person, was replicated and found to be very similar on the second test.

1.5

The bulk of those neurologically affected at Angurugu come from clan L, though clan Y cases from Caledon Bay resemble them. Unaffected clan members keep alert, with apprehension, for herald signs of the disease. They describe that the voice grows softer, and that the capability to laugh out loud may be lost. Then the body feels weak and weary. As the condition progresses the person seems stiff, becomes clumsy, and is apt to lurch when turning. Judgement of distance may make driving a car risky. Focusing eyes may be difficult. Some cases advance, while others keep stationary; this divergence is illustrated by two brothers at Angurugu. Early mission contacts noted some deformities (Fig.2).

The clinical signs have been fully described elsewhere (1)(1). The picture is a disorder of pyramidal and spinocerebellar function, with oculomotor loss. Parkinsonism is not an early sign, but can become severe in advanced cases, shown by the "fixed grin".

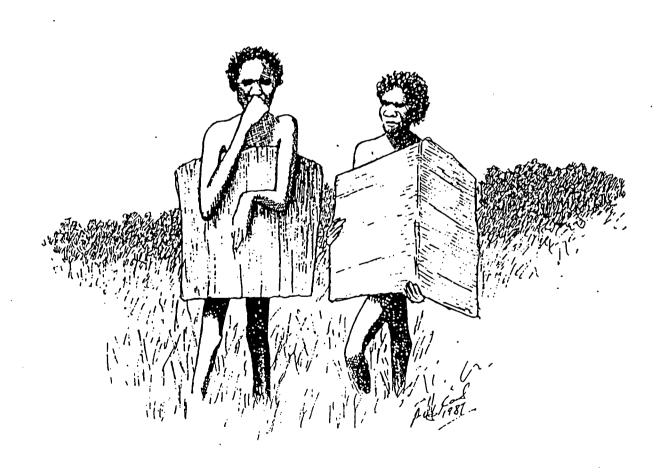
The motor problems were dramatically improved in cases treated by the writer at Prince Henry Hospital by L Dopa (Sinemet). This improvement was verified by trained neurological observers, who assessed films of the patients, shown to them out of chronological order (Table 4), and without providing information of the disease or treatment. Unfortunately, as in the cases described by George Cotzias, improvement was not sustained, so that L Dopa was relinquished after some months, to the disappointment of all concerned.

Clan B shows a condition that may or may not be related to the adult disease. It is a congenital disorder becoming progressively apparent after birth. The subjects are locally called "bird people" after a fancied resemblance to wading birds such as the heron. The condition is not progressive. The subject shows wasted limbs and remarkably lax ligaments of the joints.

A third condition, pandemic in the Angurugu community involves outbursts of violence. It is dealt with by the law rather than by medicine. It inevitably invites comparison with Californian attacks of violence in the prisoners reported by Gottschalk et al [17], mentioned earlier. Many community members become unduly irritable, quickly prone to crime. There is an exorbitant amount of brawling, leading to injuries such as fractures or lacerations, and in unlucky cases, homicide. Measured by the inordinate amount of police interventions, arrests and imprisonment, this arousal to violence surpasses that of any other indigenous community. Some observers of this temperamental violence seem satisfied with socio-cultural explanations. One indigenous health worker described the central problem of his race in such terms. His people, forced to live now in close company, lacking personal fulfilment, are highly sensitive to issues of jealousy. He designates the problem of



FIGURE 2



Early contact at the Mission. The deformity of the arm and hand of the woman on the left is particularly evident in the photograph from which Billy Reid worked - (Cole, K., 1975: Croote Evlandt, p.15).



Table 4: Gait Before and After Sinemet

Sign		"Blue" film (After)	"Red" film (Before)
1.	Lurching from loss of balance	4.79	7.77xxx
2.	Slow recovery from lurching	4.43	8.0 xxx
3.	Errant (side to side) course down corridor	5.29	7.07xxx
4.	Laborious (slow) course down corridor	4.71	7.21xxx
5.	Separation of feet apart, for balance	4.93	7.07xx
6.	Separation of arms from sides, for balance	5.85	6.67NS
7.	Laborious (slow) turning on th spot	e 5.86	8.43xxx
8.	Awkward (ataxic) turning on th spot	e 5.93	8.57xxx
9.	Fixity of gaze on floor	5.79	7.43x
10.	Patient's apparent discomfort, concern, or anxiety	3.86	5.36xxx

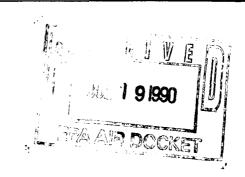
The scores in each column represent the average scores of the fourteen (14) observers, who made their judgements independently of one another. The T-Test was applied to each pair of scores.

$$x = p < .01$$

xx = p < .05

xxx = p<.001

NS = not significant



Other emic observers differ. The chairman of the Angurugu County Council, Mr. Murubuda Wurramarrba, attributes the cause to "manganese on top of alcohol", (11). Whereas other communities have become more peaceful, violence in his own has increased. He says that alcohol abuse alone cannot be blamed. Before alcohol came to Angurugu, many Blue Mud Bay people, including his own father and grandfather showed a violent disposition. They were "killers", he said.

Inevitably, this assessment has attracted the lively interest of those concerned with the trait of violence in Californian prison inmates, revealing high manganese markers in their hair (17)(18).

DISTINCTIVE FEATURES CONFRONTING EARTH DWELLERS IN A MANGANESE ECOLOGY

Earth-dwellers living in a manganic/aluminium ecological zone are exposed in a radically different manner from miners or industrial workers. These differences must be borne in mind before too prompt comparisons, or contrasts, are made between the disease patterns of the two cohorts (18)(11).

Firstly, earth-dwellers are exposed to the dust for life, from birth onward, for 24 hours per day, unlike workers who encounter it for only 8 hours per day when adults, and who customarily wash it off at the end of the day. Secondly, with earth-dwellers, women and children are exposed as well as men. Women are able to transmit high blood levels of toxin across the placenta to a defenceless foetus. Children are known to be specially susceptible to entry of manganese into the nervous system, because of the permeability of the blood-brain barrier at young ages (1).

Thirdly, in earth-dwellers, co-factors may be active that enhance, or alter, the effect of manganese in the brain. At Blue Mud Bay, these co-factors include low iron levels, severely reduced in some cases of the prevalent hookworm anaemia that troubles those in bare feet. Soil and water are high in aluminum. Low levels of calcium are widespread. It is a possibility that low calcium levels may comprise the common factor in the Western Pacific foci, scattered along this longitude of 133 degrees east, of A.L.S. and parkinsonism (11)(11). Here again, the "soil" affects the health of its occupants, when they live at soil level.



DISCUSSION

Unlike Canada and the U.S.A., Australia has not fostered Departments of Transcultural Psychiatry within its universities, designed to research and help the adaptational problems of the indigenous peoples. Perhaps the indigenous people, along with others, are too sensitive to the old stigma of psychiatry and fail to see in it any relevance, and have not reacted in the manner of their equally stressed brothers, American Indians.

Observation of the kind presented in this paper, intended to inform health personnel in Australia, were carried out during spare time available from city duties, such as holidays. This periodic work has been going on for ten years, but is still far from complete. The employment of full-time research officers on the scene should continue to clarify matters, and expedite solutions for those effected.

The prescription that the present worker offered the local people was brief. Potentially susceptible people should try to relocate to settlements where manganese levels are less high. This not as easy in the Blue Mud Bay as it may seem: even the food chain fish and shrimps - may be loaded with the element. Added to this, the imperative question remains: who are "susceptible"? It is hoped that this can be clarified by the planned collaboration between Canadian ecotoxicological experience and our own, now being arranged.

Neither groups would be prepared to neglect the old axiom, proposed in 1837 by Commander J. Lort Stokes, Captain of H.M.S. Beagle, with which this paper began:

"The natives of Australia vary as strangely as its soil".



ACKNOWLEDGMENTS

2Ten years ago, the Council of Angurugu Community of Groote Eylandt invited the writer to observe the community and the patients suffering from neurological or neuropsychiatric difficulties. The invitation was made because of the writer's familiarity to them as a medical visitor to nearby Elcho Island in Arnhem Land, and his honorary editorship of the national journal The Aboriginal Health Worker. During this decade, the Angurugu Community has afforded every assistance possible, during the necessarily brief observation periods. The Church Missionary Society has been equally hospitable. Various associates of the Groote Eylandt Mining Company have been most helpful, especially Mr. Jack O'Hare, former safety officer, now in retirement on the The nurses and Aboriginal health workers have provided island. essential help, including accommodation at the community health The CSIRO from Lucas Heights in Sydney, led by Dr T.M. Florence, made invaluable ecological measures, some of which are cited in this paper.

From the medical quarter, support has been freely given by colleagues of Prince Henry Hospital, Sydney, especially L.G. Kiloh and A.K. Lethlean. The National Health and Medical Research Council provided a grant which permitted the research allocation of Dr. Charles Kilburn, paediatrician, in the community. The Health Department of the Northern Territory provided support and encouragement, especially from the local division of East Arnhem Land, administered from Nhulunbuy by Mrs Margaret Sheridan. Accommodation has also been freely provided at the Gove District Hospital, where the district medical officers, such as Dr. Henning Madsen, have been closely interested in this research problem, and personally helpful to an intermittent Southern visitor.

Presently, thanks are due to community, company and health Department for negotiating the appointment of Dr Tim Burt to continue the research on a full-time basis, with the help of Darwin colleagues such as Dr. B. Curry. The writer is grateful to all, but especially to members of the suffering L clan, for whom his observation created at least some hope, and in part comfort. Good wishes are extended to Dr. Tim Burt for his continuing conduct of this unusual responsibility with the help of Dr John Donaldson, international cosultant in manganese toxicology from Ontario, Canada.



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